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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,636	10/26/2001	Jose de Jesus de la Fuente	67686/00-602	1974

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EXAMINER	
MINNIFIELD, NITA M	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,636	DE LA FUENTE ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-15 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 2 Sheets

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 8, 2004 has been entered.

2. Applicants' amendment filed April 8, 2004 is acknowledged and has been entered. Claims 1-8 and 16 have been canceled. New claims 21 and 22 have been added. Claims 9, 12, 14, 15, 17, 19 and 20 have been amended. Claims 9-15 and 17-22 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment and/or comments with the exception of those discussed below.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 9-15 and 17-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite because they contain the abbreviations "MSP1a". Full terminology should be in each instance in the claims without the additional use of redundant abbreviations in parentheses or otherwise. Correction is required.

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 9-15 and 17-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-12 of copending Application No. 10/285319. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both disclose a vaccine comprising recombinant MSP1a and/or subunits or tick cells and methods of using these vaccines.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 9, 12-15, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by McGuire et al (5549898) in light of McGarey et al, 1994 (Infection and Immunity; 62/10:4587-4593).

McGuire et al discloses a purified antigenic surface protein of *A. marginale* and that the antigen is useful as a vaccine component for protecting mammals against infection by *A. marginale* (abstract; col. 1; col. 6; col. 17; claims). This protein has a molecular weight of 105 kD (figures; col. 2; col. 4). The protein has been produced by recombinant DNA techniques (cols. 4-8). McGuire et al disclose that the vaccine also contains adjuvants or any other suitable pharmaceutically acceptable carrier or diluent (col. 8). McGuire et al discloses other antigenic (i.e. immunogen from *A. marginale*) and those they are also of use (col. 4). McGuire et al disclose that in addition to the native proteins isolated and purified from *A. marginale*, the antigens and immunogens according to this invention can comprise active agents formed of one or more such proteins, polypeptide fragments of such proteins, or one or more immunologically similar proteins or polypeptides produced by synthesis or genetic engineering (col. 4). McGuire et al indicate that the purified antigens can be made by recombinant means or artificially synthesized (col. 6). McGuire et al disclose the use of Oklahoma isolates (col. 18).

It is noted that McGarey et al discloses that the MSP1a has a molecular weight of 105 kD (abstract).

The prior art vaccine composition and methods appear to be the same or similar to that claimed by Applicants. Since the Patent Office does not have the facilities for examining and comparing applicants' vaccine composition and methods with the vaccine composition and methods of the prior art reference, the

burden is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed vaccine composition and methods of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant's arguments filed August 14, 2003 have been fully considered but they are not persuasive. Applicants have argued that the new claims are directed to vaccines comprising recombinant MSP1a surface protein antigen in combination with an immunogen derived from *A. marginale* and related methods. However, as set forth above, the prior art does disclose the MSP1a and another protein (i.e. immunogen) from *A. marginale* as well as the related methods.

The rejection of claims 9, 12-15, 19 and 20-22 under 35 U.S.C. § 102(b) as anticipated by McGuire et al (5549898) in light of McGarey et al, 1994 (Infection and Immunity; 62/10:4587-4593) is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 9, 12-15, 19 and 20 under this statutory provision, as set forth in the last Office action.

Applicants' have asserted that McGuire et al. is about the immunogenicity of purified MSP1 complex. The patent teaches that purified MSP1 complex may be sufficient as a vaccine to impart protective immunity against *A. marginale*; but by its own admission the patent fails to demonstrate the immunogenicity of either native or recombinant MSP1a. Consider first the following excerpt from McGuire et al., which establishes the correspondency of MSP1 complex to McGuire et al.'s protein designated "Am105"; MSP1a to Am105U; and MSP1b to Am105L. It is noted that the patent at col. 13, lines 15-20, which Applicants cite

in the amendment indicates that Am105U is sometimes referred to as MAP1a, Applicants' invention.

Applicants have asserted that McGuire et al.'s reported immunization studies involved only the purified MSP1 complex (Am105) (col. 17, lines 8-51) and that notably, only five Am105 vaccinates were studied, and, of the five, only two attained complete protection. However, the abstract of McGuire et al indicates that the antigen is useful as a vaccine component for protecting mammals against infection by *A. marginale* (abstract). Further, the example set forth in column 17 and Table 4 of McGuire et al discloses that protection was provided against *A. marginale* infection in the immunized calves as compared to the controls. Even though only 2 of the 5 were completely protected, the others were protected from infection longer (i.e. days) than the controls. "The significant elongation of the prepatent period (days until infection was detected), significant reduction in parasitemia, significant difference in PCV, and complete protection in 2 of 5 Am105 vaccinates relative to calves immunized ovalbumin indicates that Am105 is capable of inducing significant protection against challenge with against *Anaplasma marginale*." (col. 17, lines 45-51). Further, the claimed invention does not specify the degree or level of protection that should be achieved by the claimed vaccine.

Applicants state that the examiner cites McGarey to show that the 105 kD protein discussed in McGuire et al. must be MSP1a. Applicants have asserted however, that McGuire et al. explicitly discloses that the purified MSP1 complex itself has a molecular weight of 105 kD (see col. 6, lines 22-24). It is noted however, that the art discloses that MSP1a has a molecular weight of 105 kD and the MSP1b has a molecular weight of 100 kD (see Vidotto et al 1994, Infection

and Immunity, 62/7:2940-2946). It would appear that MSP1a, which has been referred to as Am105, appears to be the same.

Applicants have asserted that while McGuire et al. reports the synthesizing of recombinant MSPI (Am105), it concludes that there are important antigenic differences between the purified and recombinant MSP1. However, it is noted that the recitation of "recombinant" is view as a process limitation and does not impart novelty or unobviousness to the claimed composition comprising the MSP1a. The source of a particular protein does not impart novelty or unobviousness to a particular protein when said protein is taught by the prior art. The purification or production of a protein by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a protein is novel and unobvious over the prior art, the protein per se, even when limited to the particular process, is unpatentable over the same protein taught by the prior art. See In re King, 107 F.2d 618, 620, 43 U.S.P.Q. 400, 402 (C.C.P.A. 1939); In re Merz, 97 F.2d 599, 601, 38 U.S.P.Q. 143, 144-45 (C.C.P.A. 1938); In re Bergy, 563 F.2d 1031, 1035, 195 U.S.P.Q. 344, 348 (C.C.P.A. 1977) vacated 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 U.S.P.Q. 529, 543 (D.N.J. 1979).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., cleavage of peptides of native MSP1a) are not recited in the rejected

claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, it is noted that the claims do not set forth a nucleic acid sequence or an amino acid sequence for the claimed MSP1a.

Applicants have asserted that McGuire et al. does not anticipate Applicant's claimed invention. By its own admission, McGuire et al. presents absolutely no evidence that either nonrecombinant MSP1a or recombinant MSP1a is, or would be, an effective immunogen. Indeed, McGuire et al. is constrained by the reported test results even to conclude that the recombinant MSP1 complex is effective for conferring protection. However, McGuire et al disclose that Am105U may be more likely to induce protection because this polypeptide contains the epitope recognized by neutralizing monoclonal antibody 22B." (col. 26, lines 45-47) McGuire et al also discloses that "The most effective vaccine against *Anaplasma marginale* may be a combination of surface proteins. These include Am86, Am61, Am36, and Am31 as well as Am105, Am105L or Am105U. We described here the cloning and expression of an *Anaplasma marginale* gene in structural and antigenic homology between cloned and native surface proteins. Since cattle are protected against *Anaplasma marginale* by immunization with Am105 purified from infected erythrocytes, these results suggest that a recombinant vaccine is feasible and provide a rational basis for its development." (col. 27, lines 27-37)

Applicants have asserted that the claimed invention encompasses a vaccine composition against *A. marginale* including recombinant MSP1a in combination with an immunogen derived from *A. marginale* and a carrier or diluent, as well as a

method for inducing protective immunity using the composition. Considering the lack of any disclosure in McGuire et al. that the administration of full length recombinant MSP1a imparts protective immunity, and further in light of the extensive explicit disclosure of McGuire et al. as relates to the uncertainty and unpredictability between the native and recombinant MSP1 investigated, the patent cannot be said to provide a reasonable expectation of success that recombinant MSP1a would be effective in conferring protection against *A. marginale*. The patent thus fails to enable the use of recombinant MSP1a as a vaccine against *A. marginale*, and, as such, the reference is insufficient to anticipate the claimed invention. See *In re Sun*, 31 USPQ2d 1451, 1453 (Fed. Cir. 1993) (unpublished) ("But to be prior art under section 102(b), a reference must be enabling.... That is, it must put the claimed invention in the hand of one skilled in the art.").

However, it is noted that a US Patent is presumed valid and enabled. Since every patent is presumed valid (35 U.S.C. 282), and since that presumption includes the presumption of operability (Metropolitan Eng. Co. v. Coe, 78 F.2d 199, 25 USPQ 216 (D.C. Cir. 1935), examiners should not express any opinion on the operability of a patent. Affidavits or declarations attacking the operability of a patent cited as a reference must rebut the presumption of operability by a preponderance of the evidence. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). Further, since in a patent it is presumed that a process if used by one skilled in the art will produce the product or result described therein, such presumption is not overcome by a mere showing that it is possible to operate within the disclosure without obtaining the alleged product. In re Weber, 405 F.2d 1403, 160 USPQ 549 (CCPA 1969). It is to be presumed also that skilled workers would as a matter of course, if they do not immediately obtain desired results, make certain experiments

and adaptations, within the skill of the competent worker. The failures of experimenters who have no interest in succeeding should not be accorded great weight. In re Michalek, 162 F.2d 229, 74 USPQ 107 (CCPA 1947); In re Reid, 179 F.2d 998, 84 USPQ 478 (CCPA 1950).

It is also noted that the pending claims, for example claim 9, recite "A vaccine composition for inducing an immune response in a ruminant, said vaccine ***composition comprising*** recombinant MSP1a in combination with an immunogen derived from *A. marginale*, wherein said vaccine composition further comprises a pharmaceutically acceptable carrier or diluent. Applicants' use of the open-ended term "comprising" in the claims fails to exclude unrecited steps and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948).

8. Claims 10, 11 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGuire et al (5549898) in light of McGarey et al, 1994 (Infection and Immunity; 62/10:4587-4593) as applied to claims 9, 12-15, 19 and 20 above, and further in view of Barbet et al 1999.

McGuire et al discloses a purified antigenic surface protein of *A. marginale* and that the antigen is useful as a vaccine component for protecting mammals against infection by *A. marginale* (abstract; col. 1; col. 6; col. 17; claims). This protein has a molecular weight of 105 kD (figures; col. 2; col. 4). The protein has been produced by recombinant DNA techniques (cols. 4-8). McGuire et al disclose that the vaccine also contains adjuvants or any other suitable pharmaceutically acceptable carrier or diluent (col. 8). McGuire et al discloses

other antigenic (i.e. immunogen from *A. marginale*) and those they are also of use (col. 4). McGuire et al disclose that in addition to the native proteins isolated and purified from *A. marginale*, the antigens and immunogens according to this invention can comprise active agents formed of one or more such proteins, polypeptide fragments of such proteins, or one or more immunologically similar proteins or polypeptides produced by synthesis or genetic engineering (col. 4). McGuire et al indicate that the purified antigens can be made by recombinant means or artificially synthesized (col. 6). McGuire et al disclose the use of Oklahoma isolates (col. 18). The prior art discloses the claimed invention except for the immunogen being tick cell culture derived *A. marginale.*

However, Barbet et al 1999 teaches a composition comprising MSP1a in PBS (materials and methods), and that the proteins have potential value in diagnostic assays and vaccine value (p. 103; p. 106). Barbet et al teaches that *A. marginale* have been grown in continuous culture in a cell line, IDE8, derived from embryos of tick *Ixodes scapularis* (p. 102). The art teaches that "[b]ecause the cell culture-derived *A. marginale* organisms were morphologically similar to organisms in naturally infected ticks, it was important to determine which surface antigens, if any, were conserved among the cell culture-, bovine erythrocyte-, and tick salivary-gland-derived *A. marginale* organisms in order to evaluate the potential of using cultured *A. marginale* for future research and for development of improved vaccines and diagnostic tests." (p. 102) Further, Barbet et al teaches that the "[p]resence of these erythrocyte-stage MSPs on cultured, animal-infective rickettsiae suggests that the cell culture-derived *A. marginale* may serve as a source of *A. marginale* of great potential value for basic and applied research. Cultures might be used, for example, to assess antigenic stability and diversity

during passage of *A. marginale* through cattle and ticks, to determine whether antigens of biological relevance are expressed selectively on *A. marginale* derived from ticks, to develop transformation systems and gene knockouts to discover rickettsial gene function, for screening of novel therapeutic agents, and for development of improved diagnostic reagents and vaccines. Use of cell culture-derived *A. marginale* may considerably reduce the need to use cattle as a source of rickettsiae." (p. 106). Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use both the isolated MSP1a antigen and other immunogens even the tick cell culture since the art teaches that the antigenic proteins are on the cell surface. The claimed invention is prima facie obvious in view of the combined teachings of the prior art absent any convincing evidence to the contrary.

This rejection is maintained for the reasons of record. Applicants' arguments filed April 8, 2004, have been fully considered but they are not deemed to be persuasive. Please see the previous rejection with regard to responses to arguments concerning McGuire et al (5549898) and McGarey et al, 1994.

9. No claims are allowed.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is

571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
June 8, 2004